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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,350	11/08/2002	Anne Clark	NCI-108US	8642

7590 06/03/2004

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EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 06/03/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,350	CLARK ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,27,32-36,41,43,44,46,47 and 53-58* is/are pending in the application.

4a) Of the above claim(s) *32-36,41,43,44,46,47 and 54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,27,53 and 55-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claims 22-24 and 27 which includes a specie election for 3-dimethylamino-1-propanesulfonic acid in Paper No. 9 is acknowledged.

Claims 33-37, 41-44, 46 and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

New claims 53-58 have been added. The elected specie reads on the structure of claim 53. Hence, claim 54 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected specie, there being no allowable generic or linking claim. New claims 53 and 55-58 will be examined with the elected Group III and the elected specie, insofar as the claims read on the elected specie.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 22-24, 27, 53 and 55-58 are presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 53 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 is drawn to an inhibitor wherein the variables k, m, t, p and q are independently 0 or 1. The claims is confusing because when each of k, m, t, p and q are zero, the variables W, A, C and Y are not present and the structure is moot. In this case, claim 53 is not claiming anything. Further, the variable q and m are in conflict when m is zero and q is 1. If m is 0, the nitrogen substituent, which is directly bonded to A , can not be present. In this case, if m is zero, then the value of q is also zero by definition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22-24, 27, 53 and 55-57 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Cik et al. (1993).

Cik et al disclose that cloned N-methyl-d-aspartate subunits can be expressed *in vitro* in HEK 293 (human embryo kidney) cells, as in claims 55 and 56. Cik et al. teach that the inclusion of 2-amino-5-phosphopentanoic acid (AP5), as in claims 27 in the culture medium increases the expression of the subunits in the cells, as in claim 24. 2-Amino-5-phosphopentanoic acid (AP5) is a synonym of 2-Amino-5-phosphonovaleric acid, specie ii of instant claim 27. AP5 also meets the structural limitations of the generic claims 53 (abstract).

Claims 22-24 describe what the cells do, but do not require any particular action by the cells. The claim require that a person culture cells that are suitable for transplantation with a compound that can inhibit amyloid formation. The cells have to be capable of forming amyloid deposits, as in claim 57, and so on. However, the claims do not require that the deposits actually be present in the claimed cells. Absent evidence to the contrary, a culture of HEK 293 cells having cloned N-methyl-d-aspartate subunits are suitable for transplantation because kidney cells inherently have receptors for N-methyl-d-aspartate. The cloned subunits disclosed by Cik et al. do not compromise the suitability of the cells for transplantation. Although Cik et al. do not disclose that AP5 is an inhibitor of amyloid deposit formation, this action is an undisclosed characteristic of a known compound. Likewise, human kidney cells are capable of forming amyloid deposits and if amyloid deposits appeared in said cells, the inherent amyloid-destroying property of AP5 would breakdown said amyloid deposits. Hence, Cik et al. meet the limitations of claims 22-24.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-24, 27, 53 and 55-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Westermark et al. (1998, abstract) in view of Copani et al. (1995) and Kisilevsky (1996).

Westermark et al. disclose that human islets transplanted into nude mice developed extensive intracellular amount of amyloid deposits (p. 546, Results, first paragraph).

Westermark et al. do not disclose contacting the human islets with a compound that inhibits or degrades amyloid deposits in human islet cells.

Copani et al. disclose that β-amyloid peptide (βAP) induces neural apoptosis in cultured cerebellar granule cells. However, Copani et al. found that co-incubation of serine-*O*-phosphate or 2-amino-4-phosphobutanoate with βAP in the cell culture, protected against βAP-induced apoptosis (abstract and page 893, Figure 3). Serine-*O*-phosphate is a synonym of *O*-phosphoserine, compound v of claim 27. The compound, serine-*O*-phosphate or 2-amino-4-phosphobutanoate, also meets the structural limitations of the generic claims 53.

As noted above, claims 22-24 describe what the cells do, but do not require any particular action by the cells. Copani et al. are silent regarding the deposition of βAP in the cells. However, said cells are capable of forming deposits endogenously. The ability of serine-*O*-phosphate and 2-amino-4-phosphobutanoate to inhibit or break-down amyloid deposits are inherent properties of the compounds. the Copani et al. state that the identification

of pharmacological agents that oppose amyloid-induced apoptosis is important for discovering therapeutic agents for Alzheimer's disease (p. 890, bottom of right column).

Kisilevsky teaches that IAPP and amyloid plaque related to Alzheimer's disease have common components (p. 76, Table 1). Kisilevsky discusses strategies for anti-amyloid therapy in all cell types such as treating affected cells with inhibitors to prevent amyloid formation or enhancing amyloid removal.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add serine-*O*-phosphate to human islets intended for transplantation in order to inhibit or remove amyloid deposits in islets. The ordinary artisan would have been motivated to do so because serine-*O*-phosphate had been shown to inhibit the deposition of βAP in kidney cells. The ordinary artisan would have had a reasonable expectation of success that serine-*O*-phosphate would inhibit or remove IAPP deposits in islet cells because all amyloid-based diseases have common components that would be susceptible to the same types of amyloid-inhibiting treatments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEAN C. WITZ
PRIMARY EXAMINER